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Chemistry & Biology

In This Issue

"My Grandfather's Axe" of the RNA World

PAGE 466

The origin of RNA is a huge problem for prebiotic chemists. Hud et al. discuss why they think it unlikely that the current RNA building blocks are the components of life's first informational polymers, comment on possible forerunners, and evaluate models for how the earliest ancestor of RNA might have assembled.

In Review: Probing Endomembrane Trafficking

PAGE 475

The essential role of the endomembrane compartments for cellular housekeeping and interaction with the environment makes it difficult to investigate with genetics tools. Mishev et al. review chemical genetics strategies to discover small-molecule trafficking modifiers and the functional insights they delivered.

Trehalose Synthase in Flux

PAGE 487

It is currently thought that trehalose synthase contributes to the biosynthesis of trehalose mycolates destined for mycobacterial cell walls. Miah et al. show that flux through this enzyme is in the reverse direction from trehalose to maltose and that the appropriate α anomer is generated for the GlgE α-glucan pathway.

Distributive Nature of JMJD2A

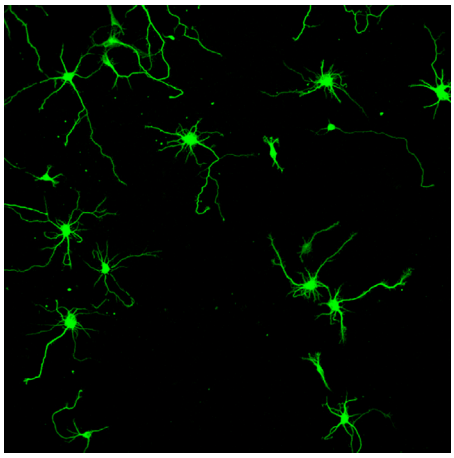
PAGE 494

Jumonji histone demethylases are critical transcriptional regulators, but major mechanistic details are missing. Shiau et al. reveal the intrinsic distributive nature of the catalytic domain of JMJD2A and suggest that JMJD2A's activity and processivity is regulated by the auxiliary domains and protein partners.

Enantioselective Way to Promote Neurite Growth

PAGE 500

Antonchick et al. develop a practical method for the tetracyclic secoyohimbane scaffold synthesis in a one-pot, multistep reaction sequence. From the resulting compounds, they identify a class of neurotrophic molecules that promote neurite outgrowth and influence the complexity of neuronal network formation.



Biosynthesis of Actinorhodin

PAGE 510

Actinorhodin (ACT) belongs to the benzoisochromanequinone class of antibiotics. Taguchi et al. show that ActVA-ORF5 and Gra-ORF21, flavin-dependent monooxygenases involved in biosynthesis of ACT and a related antibiotic, catalyze oxygenations at two different carbons in the same substrate, which is rarely seen.

G-Quadruplex Hearts GTP

PAGE 521

RNAs that bind small molecules have been implicated in a variety of regulatory and catalytic processes. Curtis and Liu search a pool of genome-derived RNA fragments for GTP aptamers. They find GTP aptamers of both RNA and DNA and show that they adopt a G-quadruplex structure and are widespread in eukaryotes.

Free Glycine Gives Asparaginase a Boost

PAGE 533

Asparaginases are enzymes that convert the amino acid asparagine into aspartic acid. Su et al. examine a human asparaginase, hASNase3, and suggest that high glycine concentrations act as a sensor for low cellular aspartic acid levels, activating hASNase3 to undergo autoproteolysis and replenish this amino acid.

Labeling Functional Tyrosines

PAGE 541

Gu et al. show that sulfonyl fluoride (SF) probes label a broad diversity of glutathione transferases in both plant and mouse proteomes. Labeling occurs specifically at functionally relevant tyrosine residues, suggesting that SF probes might point to functionally important residues in target proteins.

Bringing Proteins Closer Together

PAGE 549

Erhart et al. develop a protein heterodimerization system based on small molecules cross-linking fusion proteins fused to Halo- and SNAP-tags (HaXS), which allow chemically induced signal transduction studies. HaXS are used for protein targeting to cytoskeleton and initiation of the PI3K/mTOR pathway and others.

Astexin-1 Lasso Peptides

PAGE 558

Zimmermann et al. investigate the recently discovered lasso peptide astexin-1 to unveil the basic principles for its unusual thermolability and to inspect the tolerance of its biosynthetic machinery. They reveal a unique lasso structure, which enables creation of a thermostable variant of astexin-1.

HCV: Check the Triglyceride Levels

PAGE 570

Fatty acid synthase (FASN) activity is indispensible for hepatitis C virus (HCV) replication. Nasheri et al. use ABPP to investigate the alterations in activity of FASN in the context of HCV. Both FASN activity and expression increase significantly during HCV replication, resulting in elevated triglyceride levels.

Channeling the Fusicoccanes

PAGE 583

Anders et al. show how fusicoccanes promote the interaction of 14-3-3 proteins with the human potassium channel TASK-3 and present a semisynthetic fusicoccane derivative (FC-THF) that targets the 14-3-3 recognition motif in TASK-3 and causes a substantial increase in the number of channels at the cell membrane.

Understanding Drug Side Effects

PAGE 594

Duran-Frigola and Aloy investigate the molecular bases of over 1600 drug side effects (SE) by analyzing the chemical structures of medicines and their interactions with human proteins. The analysis provides mechanistic insights for most SEs and emphasizes the need to blend biology and chemistry perspectives.

From Electrophoresis to Sumoylation Inhibitors

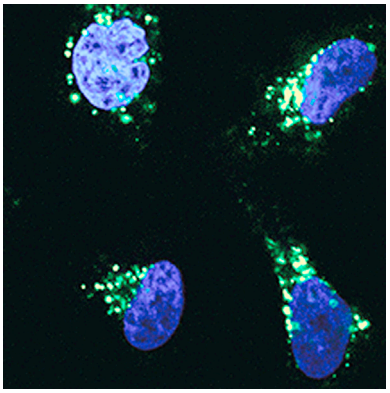
PAGE 604

Sumoylation is an area of emerging interest with broad implications. Kim et al. describe an electrophoretic mobility shift assay to probe SUMO conjugation and the discovery of 2-D08 as an inhibitor of protein sumoylation. 2-D08 inhibits the transfer of SUMO from the E2 to the substrate in vitro and in cancer cells.

Probes for Endocytosis

PAGE 614

Cells use endocytosis to absorb polar molecules and alter the concentration of cell-surface receptors. Levine et al. design a fluorogenic lipid that is used to monitor endocytosis in live human cells. They document an intrinsic difference in endocytic rate between cancer and noncancerous cells from the same patient.



Deadly LOV2

PAGE 619

Light-perception is indispensable for plants to respond adequately to external cues and is linked to proteolysis of key transcriptional regulators. Renicke et al. engineer a photosensitive LOV2 domain-based degron module and transfer the principle of light-regulated degradation to nonplant organisms.

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